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APPLICATION NUMBER: *60/514,768*
FILING DATE: *October 27, 2003*
RELATED PCT APPLICATION NUMBER: *PCT/US04/17649*

Certified by

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.	EV322656729US

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Feiling	Wang	Medford, Massachusetts

☐ *Additional inventors are being named on the _____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

COHERENCE-GATED OPTICAL GLUCOSE MONITOR

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☐ Customer Number _____ → *Place Customer Number Bar Code Label here*

OR *Type Customer Number here*

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ENCLOSED APPLICATION PARTS *(check all that apply)*

- ☑ Specification *Number of Pages* 6
- ☐ Drawing(s) *Number of Sheets*
- ☐ Application Data Sheet. See 37 CFR 1.76
- ☐ CD(s), Number
- ☐ Other (specify)

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

- ☐ Applicant claims small entity status. See 37 CFR 1.27.
- ☑ A check or money order is enclosed to cover the filing fees
- ☑ The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 50-1798
- ☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE AMOUNT ($): $160.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

- ☑ No.
- ☐ Yes, the name of the U.S. Government agency and the Government contract number are: _____

Respectfully submitted,

SIGNATURE _____

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Date 10/27/2003

REGISTRATION NO. *(if appropriate)* 36,610

Docket Number: TOM-0002PR

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

PATENT
Attorney Docket No.: TOM-0002PR
Customer No.: 29344

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Feiling Wang
Filing Date: Herewith
Title: COHERENCE-GATED OPTICAL GLUCOSE MONITOR

CERTIFICATE OF MAILING UNDER 37 C.F.R.§ 1.10

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Sir: TRANSMITTAL LETTER

Enclosed herewith for filing in the above-identified provisional patent application please find the following listed items:

1. Provisional Application Cover Sheet;
2. Provisional Patent Application including six (6) pages of specification;
3. Check in the amount of $160.00 to cover application filing fee; and
4. Return Postcard.

In connection with the foregoing matter, please charge any additional fees which may be due, or credit any overpayment, to Deposit Account Number 50-1798. A duplicate copy of this letter is provided for this purpose.

Respectfully submitted,

Date: October 27, 2003

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Invention Disclosure: Coherence-Gated Optical Glucose Monitor

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1. Description of Invention

The invention is concerned with a method and apparatus to monitor the glucose level of diabetes patients with an optical and noninvasive technique.

Presently, dependable glucose monitors rely on taking blood samples from diabetes patients. Repeated pricking of skin can cause considerable discomfort for patients. It is therefore desirable to monitor the glucose level in a noninvasive manner.

It is well known that glucose in blood possesses "signature" optical absorption peaks in a near-infrared (NIR) wavelength range. It is also appreciated the main obstacle in noninvasive monitoring of glucose is due to the fact that a probing light beam interacts, in its path, with various types of tissues and substances which possess overlapping absorption bands. Extracting the signature glucose peaks amongst all other peaks has proven difficult.

This invention addresses the difficulty through "coherence gating", a technique by which one can acquire the absorbance spectrum of a particular and designated layer beneath the skin surface. For glucose monitoring, the designated layer is preferably the dermis layer where glucose is concentrated in a network of blood vessels and interstitial fluid, as shown in Fig. 1.

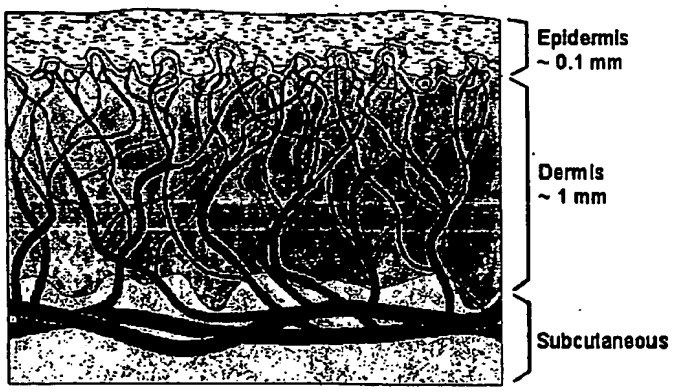

Figure. 1

The coherence gating is accomplished by the use of a low-coherence interferometer. There are many possible optical configurations for the low-coherence interferometer. Figure 2 shows one design based on a Michelson interferometer.

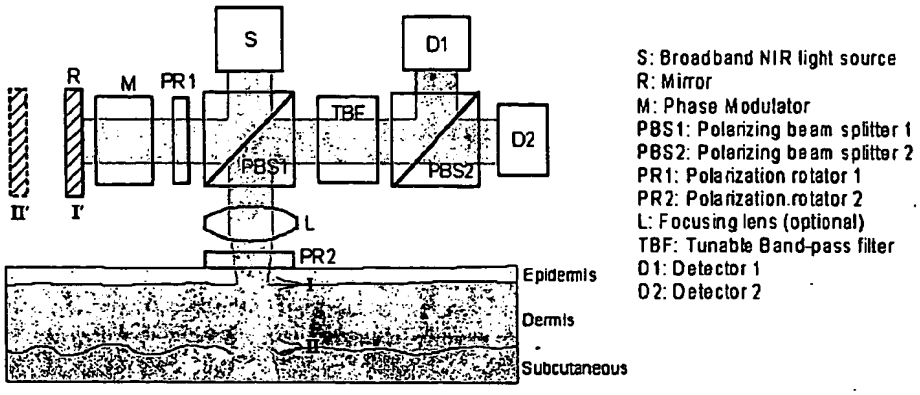

Figure 2

In the design shown, the light source emits broadband NIR radiation covering the characteristic absorption peaks of the glucose. The polarizing beam splitter, PBS1, splits the light into two parts which are mutually orthogonal in polarization to one another. While one part is directed towards a mirror, R, to be the reference beam the other is incident on the skin of a patient. The two polarization rotators, PR1 and PR2, render the polarization states of the two reflected beams orthogonal to their original states so that they are recombined at PBS1 and propagate towards the detection subsystem. The tunable bandpass filter, TBF, allows a variable portion of the spectrum in the reflected beams to reach the detectors. The movable mirror can be positioned so that its distance from PBS1 matches that between PBS1 and a desirable interface in the skin. Due to the low coherence, only the reflected (or backscattered) light originated in the vicinity of the matching interface can form interference fringes with the reference beam. Temporal interference fringes (intensity oscillation) can be generated with the help of the phase modulator.

For the simplicity of description let us assume that the wavelength dependent attenuation coefficient of the epidermis layer is $\mu_e(\lambda)$ and that of the dermis $\mu_d(\lambda)$. These attenuation coefficients are closely related to the absorbance spectra of the layers. Let us further assume that the tissue in the vicinity of interface *I* (*II*) possesses an effective reflection coefficient r_I (r_{II}). Interface *I* separates the epidermis and the dermis; and interface *II* separates the dermis and the subcutaneous tissues.

Let us first position the mirror at *I'* to approximately match interface *I*. The reflected light originated around the interface creates an interfering echo whose amplitude is given by

$$A_I(\lambda) = r_I e^{-2\mu_e(\lambda) z_e} \qquad (1)$$

where z_e is the thickness of the epidermis. Now if we relocate the mirror to *II'* to approximately match interface *II*, r_{II} gives rise to a different interfering echo whose amplitude is given by

$$A_{II}(\lambda) = r_{II} e^{-2\mu_e(\lambda)z_e - 2\mu_d(\lambda)z_d} \tag{2}$$

where z_d is the thickness of the dermis. With the use of the phase modulator these echoes interfere with the reference and produce proportional intensity oscillations measurable by the detector. To acquire the absorption characteristics of the dermis one can divide Eq. (2) by Eq. (1) to obtain

$$\frac{A_{II}(\lambda)}{A_I(\lambda)} = \frac{r_{II}}{r_I} e^{-2\mu_d(\lambda)z_d} \tag{3}$$

We have thus acquired, with Eq. (3), the absorption characteristics of the dermis layer only. The absorbance spectrum of the dermis is closely represented by coefficient $\mu_d(\lambda)$ because of the weak wavelength dependence of scattering.

It is known that the superficial epidermis layer, owing to its pigment content, is the dominant source of NIR absorption. Because of the absence of blood, however, the epidermis yields no useful information for glucose monitoring. With the invented method we can acquire solely the absorbance spectrum of the dermis layer by rejecting the absorptions of the epidermis and the subcutaneous tissues. An additional advantage is from the fact that dermis exhibits less temperature variation compared to the epidermis. It is known that surface temperature variation causes shifts of water absorption, hampering glucose monitoring.

In the above discussion it has been assumed that the pass band of the tunable filter is broad enough to facilitate the coherence gating and at the meantime narrow enough to resolve the characteristic glucose peaks. Let us now examine whether the assumption is reasonable and practical.

It is known that some predominant glucose absorption peaks reside in a wavelength range between 1 and 2.5 microns, as shown in Fig. 3. The width of these peaks are approximately 150 nm. To resolve the peaks let us choose the bandwidth of the tunable bandpass filter to be around 30 nm. The depth resolution (gating ability) is determined by the following equation:

$$\frac{2\ln(2)}{\pi}\frac{\lambda_o^2}{\Delta\lambda} = 60\mu m \tag{4}$$

The thickness of the epidermis is typically 0.1 mm and that of the dermis typically 1 mm. The above analysis (Eq. (4)) indicates that the coherence gating technique described above can comfortably resolve both the absorption peaks and the skin layers. It is therefore feasible to isolate the absorbance spectrum of the dermis layer from the epidermis and the subcutaneous tissues.

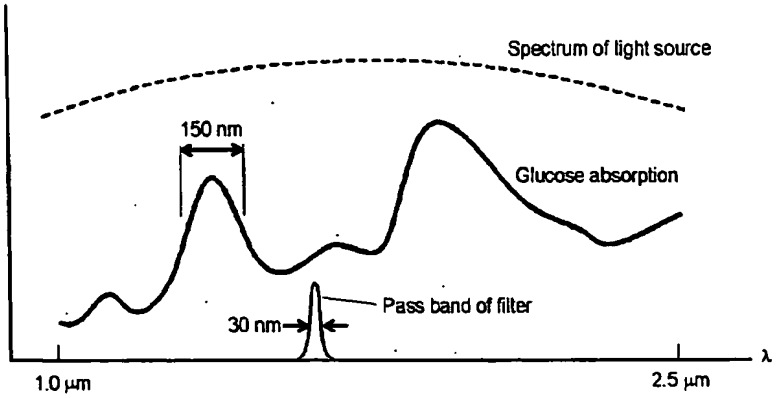

Figure. 3

To acquire the absorbance spectrum of the dermis layer one may operate the apparatus shown in Fig. 2 in this sequence: 1) locate the mirror at *I'* so that its distance matches the interface separating the epidermis and the dermis layers (position *I*); 2) scan the tunable bandpass filter across the span of the glucose signature peaks while recording the amplitude of the light intensity oscillation so that Eq.(1) is acquired; 3) relocate the mirror to *II'* so that its distance matches the interface separating the dermis and the subcutaneous tissues (position *II*); 4)repeat the process of step 2) so that Eq.(2) is also acquired. The absorbance spectrum of the dermis can be found by using Eq.(3). It should be appreciated that additional signal processing is necessary in order to determine the glucose concentration from the measured absorbance spectrum of the dermis.

The tunable bandpass filter can be one of the following devices: an electro-optically tunable filter, a rotatable fixed bandpass filter or a rotatable grating. The polarization rotators in the design can be quarter-wave plates or Faraday rotators. The movable mirror can be replace by a non-mechanical device such as a liquid-crystal cell or a combination of polarization rotators and birefringent crystals.

It should be appreciated that the use of the two detectors along with the second polarizing beam splitter, PBS2, facilitates a differential detection scheme for high signal to noise ratio. It is obvious that one can simplify the design to include a single detector with a linear polarizer.

2. Embodiment with Non-polarized Beams

It is not necessary to arrange the polarization of the light beams in the way described above. An alternative optical configuration for the same purpose is shown in Fig. 4. In this design the polarizing beam splitter is replaced by a non-polarizing beam splitter. The polarization states of the light beams can be arbitrary. With this design, however, only half of the light energy reaches the detector.

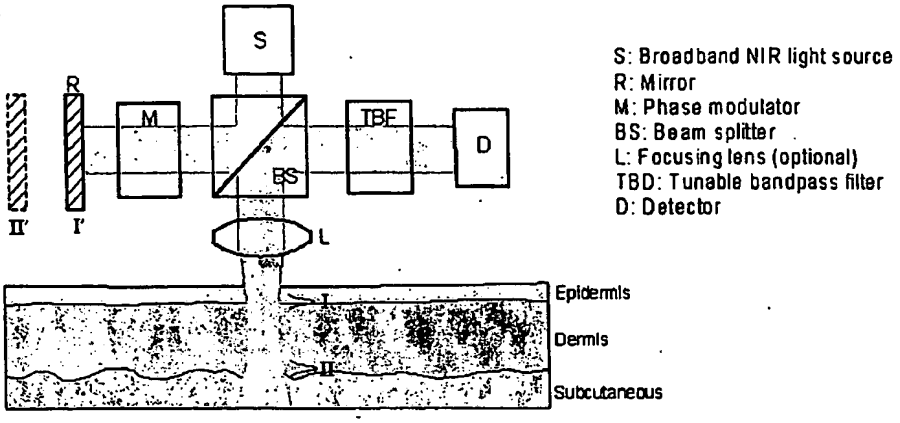

Figure 4

3. Embodiment with Detector Array

The absorbance spectrum can also be resolved by a dispersive device and a detector array instead of the tunable bandpass filter. In the design shown in Fig. 5, a reflective grating is coupled with an array of detectors. With this design the speed of data acquisition can be substantially increased through parallel processing. This design can also be reconfigured to accommodate polarized light beams, similar to what shown in Fig. 2.

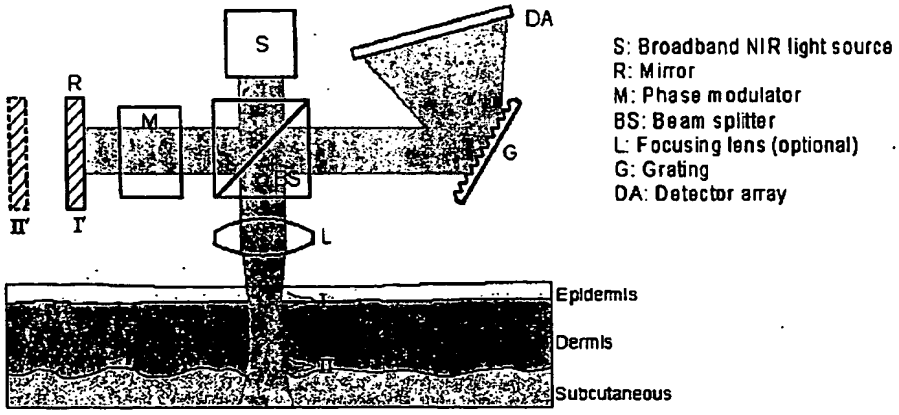

Figure 5

4. Embodiment without Spectrum Analyzer

The absorbance spectrum of the substances may also be acquired by means of post-detection signal analysis without the help of a tunable bandpass filter or a grating with detector array. This simplifies the design shown in Fig. 2 to that in Fig. 6. The same simplification can be applied to the non-polarizing version shown in Fig. 4.

Without a spectrum analyzer the absorbance spectrum of the tissues may be directly calculated from the intensity oscillation created by the interfering beams of the whole spectra. Certain mathematical transformations, such as a suitable wavelets transformation, may be adopted for such task.

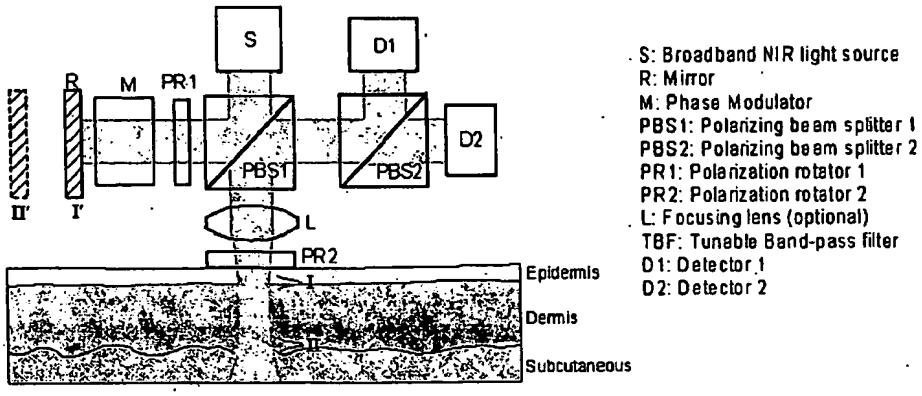

Figure 6